CRL for Cereals and Feeding stuff
National Food Institute
Danish Technical University

Validation Report 1

Determination of pesticide residues in cereals by LC- MS/MS

(internal method no. FP086.1)

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Approved by:

CONTENT:

1. Introduction

This report is valid for the validation of 51 pesticide residues in cereals, internal method no. FP086,- 'Determination of pesticide residues in fruit , vegetables and cereals by LC-MS/MS'. The validated pesticides are ionised both by positive and negative electrospray. The method is a multiresidue method which is quick and easy, due to the low amount of sample preparation.

2. Principle of analysis

The sample is milled and homogenised. 3 g. of sample is weighed and added 7 g. of water. The sample is allowed to stand for about 30 min. The sample is then added a mixture of methanol-ammoniumacetat-acetic acid and extracted by ultrasonication for 30 min. Extraction is followed by centrifugation and the supernatant is filtered into HPLC vials. The pesticide residues are separated on a reversed-phase column and detected by tandem mass spectrometry (MS/MS) by electrospray (ESI). The validation includes pesticides determined with both positive and negative ESI. $^{13}C_6$-carbaryl was used as internal standard for quantification. All pesticides were detected in

the multiple reaction monitoring mode (MRM). For each pesticide precursor ion and 2 product ions (where possible) were determined. One product ion for quantification and one for qualification. The MRM transitions for the pesticides and degradation products sought validated are given in appendix 1.

3. Validation Design

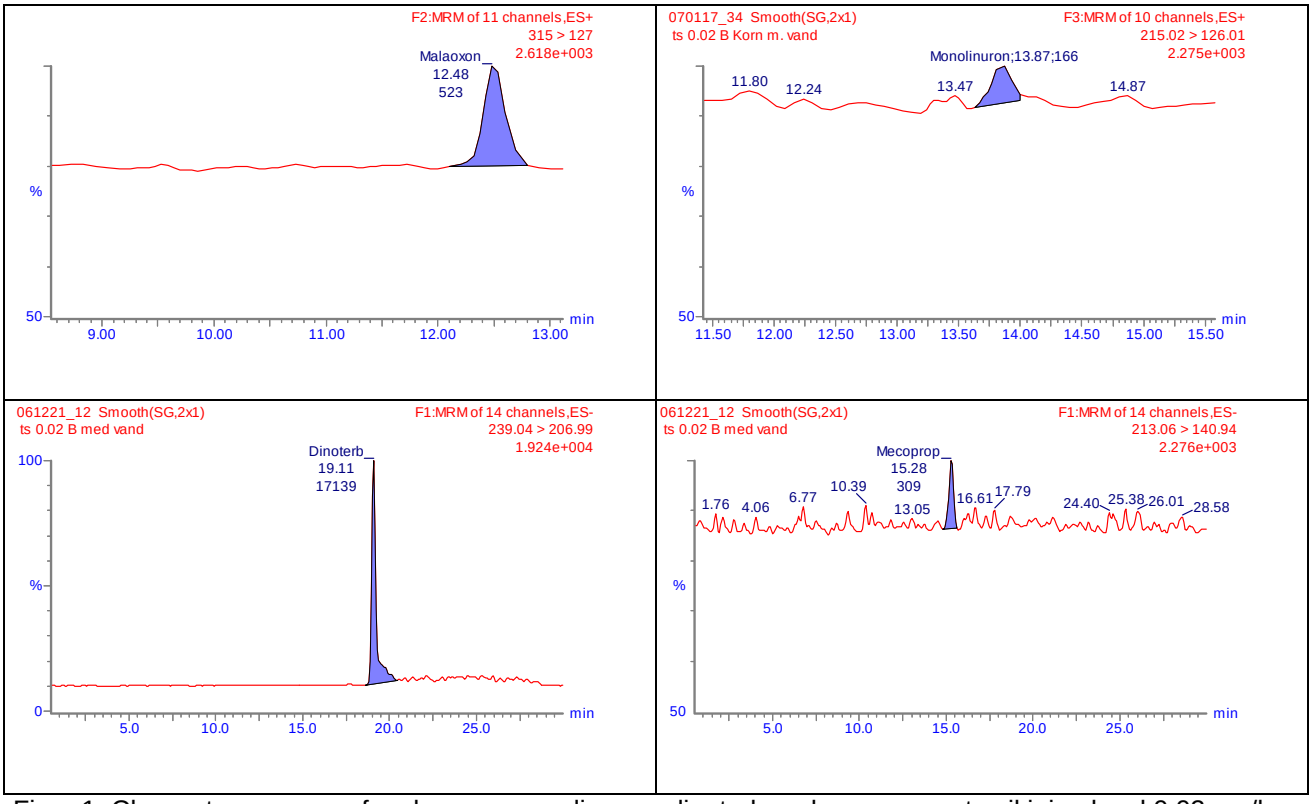
The method is validated on wheat. The recovery tests were all on organic grown wheat flour. 98 pesticides and degradations products were sought validated (appendix 1). It should be mentioned that it was not possible to distinguish between dichlorprop and dichlorprop-P, nor was it possible to distinguish between mecoprop and mecoprop-P. Therefore these compounds are only counted for one.The pesticides were spilt into two standard solutions, one for the ESI positive ionisation and one for the ESI negative ionisation. It may be possible to mix the standard solutions and then measure the same standard in two runs, one for positive ionisation and one for negative ionisation. It was decided not to measure both positive and negative ionisation in the same run, due to the fact that the MS/MS system might loose sensitivity when changing from positive to negative in the same run. And that the run in the positive mode was already fully occupied (with regard to the capacity of the MS/MS system).

Every recovery test was performed as double determinations at three concentration levels, 6 samples and 1 blank, in total 7 samples. This was repeated four times. The tests were done on different days by two different technicians.

Test	0 mg/kg	0.02 mg/kg		0.04 mg/kg		0.2 mg/kg	
1	X	X	X	X	X	X	X
2	X	X	X	X	X	X	X
3	X	X	X	X	X	X	X
4	X	X	X	X	X	X	X

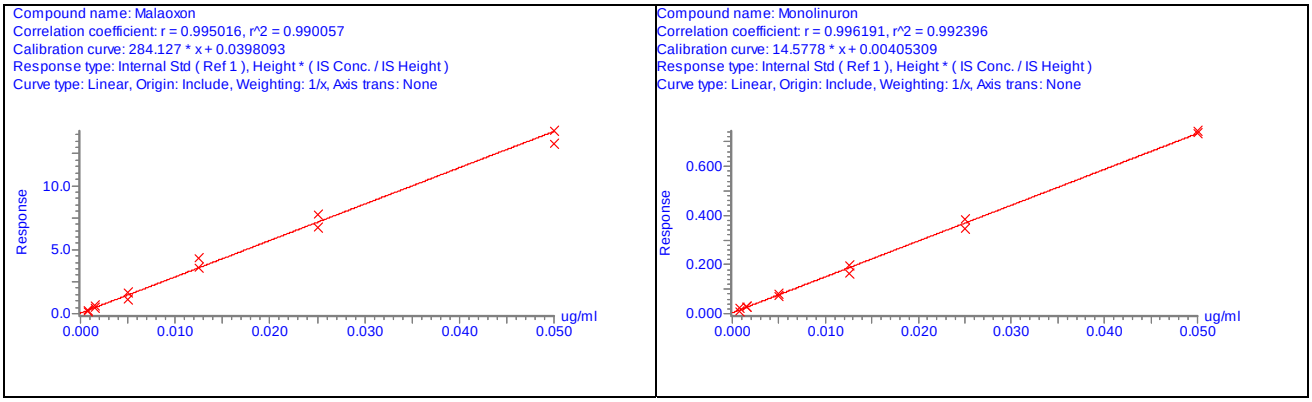
4. Chromatogrammes and calibration curves

The MRM detection of the pesticide residues are parted in 7 windows according to retention times, windows were partly overlapping. In figure 1 examples of chromatogrammes are given.



Figur 1. Chromatogrammes of malaoxon, monolinuron, dinoterb and mecoprop at spikining level 0.02 mg/kg.

5-point matrix-matched calibreation curves were used for quantification. The concentration were 0.0015, 0.003, 0.01, 0.025 and 0.050 µg/ml. The quantification was performed from the mean of two calibration curves surrounding the samples. $^{13}C_6$-carbaryl was used as internal standard. Examples of calibration curves may be seen in figure 2.



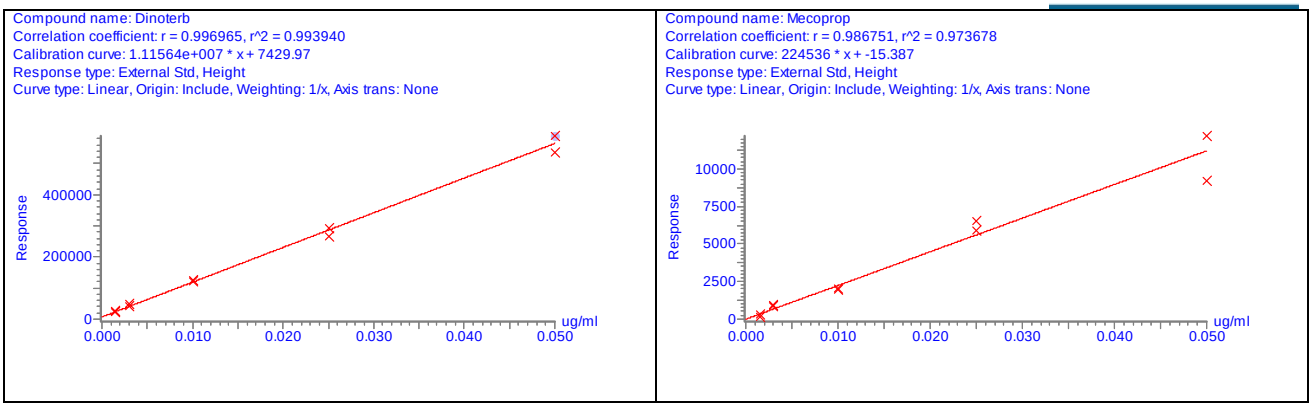


Figure 2. Examples of calibration curves for malaoxon, monolinuron, dinoterb and mecoprop (concentrations from 0.0015-0.05µg/ml)

5. Precision – Repeatability and reproducibility

Repeatability and in-house reproducibility were calculated for all pesticides and degradation products on all three spiking levels.

Repeatability is given as the relative standard deviation on the result from two or more analysis at the same sample, done by the same technician, on the same instrument and within a short period of time. Repeatability is calculated from the double determinations.

In-house reproducibility is the relative standard deviation on the result from two or more analysis done on the same sample but by different technicians and within a larger period of time. Reproducibility includes the variation between double determination and variations between the different series of analysis. .

Repeatability and reproducibility were calculated as given in ISO 5725-2[1].

Appendix 2 shows the repeatability and the in-house reproducibility for the validated pesticides and degradation products. Repeatability and reproducibility varies for the individual pesticides. At the lowest spike level 0.02 mg/kg the repeatability and reproducibility is generally higher than at higher spike levels (0.04 and 0.2 mg/kg). For some pesticides the reproducibility is >30%, on explanation may be the sensitivity of the instrument varies throughout a run, and is not completely compensated for by the use of internal standard. Due to the high amount of samples that are to be analysed by this method we chose not to use standard addition for quantification. This would improve the precision and may be considered to use in cases of exceedances of the MRL.

6. Accuracy – Recovery.

The accuracy is determined by recovery, samples are spiked at three concentration levels. In appendix 2 recovery, repeatability, reproducibility and limit of detection (LOD) are given for the validated pesticides and degradation products. For most of the pesticides the recovery are in the range of 70-110% for all three concentration levels (0.02mg/kg, 0.04 mg/kg and 0.2 mg/kg) even more are in the range of 60-120%.

In general the recoveries are not very good, which might be due to the low amount in of sample, i.e. 3 gram. Furthermore the dry matrices like wheat flour are known to be difficult matrices in pesticide residue analysis, due to larger matrix effect. Previous experiments (not published) have shown that there might be a connection between the time the samples are stored in the refrigerator or at room temperature before LC-MS/MS detection (and recovery). Therefore it is recommended that [1)] The time where the samples are not frozen should be minimised; [2)] That time from extraction to transfer to vials is as short as possible and [3)] That samples either are analysed directly or stored in freezer until analysis.

7. Limit of detection, LOD

Detection limits (LOD) is calculated from the results at the lowest accepted spike level, as 3 times the standard deviation (absolute recovery).

The detection limits are given in appendix 2. Detection limits are in the range 0.006 mg/kg - 0.135 mg/kg. The lowest calibration level (LCL) was 0.0015µg/ml corresponding to LOD at 0.006 mg/kg. However most of the LODs are above 0.01 mg/kg and may need to be lowered for the method to be used for babyfoods.

8. Selectivity and specificity

LC-MS/MS is a highly selective detector, and thereby highly specific. For quantification of the pesticide residues a secondary product ion is used. Transitions are given in appendix 1, first transition is used for quantification, whereas second transition is used for qualification..

9. Conclusions and remarks

An LC-MS/MS method for the determination of pesticide residues in cereals has been validated for 51 pesticides and degradation products. The method is based on methanol-ammoniumiumacetat-acetic acid extraction by ultrasonication. For 40 pesticides the ionization was done by ESI in the positive mode, and for 11 pesticides the ionization was ESI in the negative mode. An overview is given below.

Recovery were in the range 57-148% for all three concentration levels. Many of the pesticides sought validated showed weak response on the LC-MS/MS and were therefore not detectable in the diluted extract (no concentration in the sample preparation). Furthermore many of the GC-troublesome pesticides and the non-polar pesticides were not extracted by the polar extraction solvent, and thereby giving poor recoveries.

Repeatability and reproducibility varies between 10->30%, however most of the values are around 20%. Both the RSD_r and RSD_R are higher than would be expected in an in-house validation. This may be due to a number of factors. It is a known fact that dry matrices like wheat flour may cause problems. Furthermore, one of the problems is that the sensitivity of the LC-MS/MS instrument varies throughout a run. The internal standard partly compensates for this, however detection by standard addition probably would improve the precision. Moreover it may be seen that validation values are much better for ESI negative compounds. This may be due to the fact that the MS/MS system only have to analyse few compound in the negative mode (13 pesticides), while in the positive mode the MS/MS system has to analyse 86 pesticides, which lowers the time the system are able to spend on each component. This however may be overcome by dividing the compounds into more standard solution, however this will increase the time for analysing one sample.

The limit of detection is determined as three times the standard deviation on the absolute recoveries at the lowest accepted spiking level. The detection limits were in the range 0.008 mg/kg - 0.135 mg/kg.

In conclusion 51 of 98 pesticides and degradation products were validated. In present method it is not possible to distinguish between dichlorprop and dichlorprop-P. Likewise it was not possible to distinguish between mecoprop and mecoprop-P. It should be pointed out that because this method is very quick and easy, due to low sample preparation and clean up, there may be compromises to be made on which pesticides and degradation products may be included.

ESI-, Validated (11 pesticides)

2-naphtoxy acetic acid	Bromoxynil	MCPA
2,4-D	Dichlorprop	Mecoprop
4-Chlorphenoxyacetic acid	Dinoterb	Thifensulfuron-methyl
Bentazone	DNOC	

Not accepted (2 pesticides)
Malein hydrazide
Triforine (might be analysed in the posivive mode)

ESI+, Validated (40 pesticides)

Acetimiprid	Fluoxastrobin	Oxycarboxim
Azimsulfuron	Iodosulfuron-methyl	Pendimethalin
Bitertanol	Iprovalicarb	Pirimicarb
Bupirimate	Isoproturon	Propamocarb
Buprofezin	Malaoxon	Pymetrozine
Clethodim	Methalaxyl-M	Pyraclostrobin
Clomazone	Methacrifos	Pyridaben
Demeton-S-methyl	Methiocab sulfoxid	Pyridaphenthion
Demeton-S-methyl sulfoxid	Methiocarb sulfon	Pyridate
Demeton-S-sulfon	Metsulfuron-methyl	Pyrimethanil
Dimethomorph	Monocrotophos	Spiroxamin
Ethoxyquin	Monolinuron	Tebufenpyrad
Fenazaquin	Ofurace	
Fluazafop-p-buthyl	Omethoate	

Not validated (46 pesticides)

Amitrole (Aminotriazole)	Fluroxypyr	Prothioconazole
Azocyclotin	Flusilazole	Pyraflufen-ethyl
Cinidon-ethyl	Flutolanil	Pyriproxyfen
Clodinafoppropargyl	Hexaconazole	Resmethrin
Clopyralid	Hexythiazox	Rimsulfuron
Cyazofamid	Imidacloprid	Tebufenozide
Cycloxydim	Jodfenphos	Tetraconazole
Cyhalofop-buthyl	Lufenuron	Thiodicarb
Cyromazine	Mepanipyrim	Triallate
Dichlofenthion	Metribuzin	Triasulfuron
Diethofencarb	Molinate	Tribenuron-methyl
Epoxyconazole	Nuarimol	Tridemorph
Fenamiphos	Oxadixyl	Triflumuron
Floroxypur	Phosmet	Trinexepac-ethyl
Fluazifop-p-buthyl	Picolinafen	
Flumioxazin	Propargite	

10. References

1. ISO 5725-2:1994. Accuracy (trueness and precision) of measurement methods and results – Part 2. Basic method for the determination of repeatability and reproducibility of standard measurement method. First edition. December 1994.
2. W. Horwitz, *Anal. Chem.*, 1982; **54**, 67A.
3. Quality Control Procedures for Pesticide Residue Analysis, Document No SANCO/10232/2006, 24/March/2006, European Commission, Brussels, 2006.

11. Appendices

Appendix 1. MRM transitions for the pesticides sought validated.

Pesticide/Metabolite	Molecular formula	Ionisation, ESI +/-	Molecular ion	precursor	Transition 1			Transition 2		
					Product	Cone voltage (V)	Collision energy (eV)	Product	Cone voltage (V)	Collision energy (eV)
2,4-D	$C_8H_6Cl_2O_3$	ESI-	[M-H]-	219	161	9	13	125	10	26
2-Naphtoxy acetic acid	$C_{12}H_{10}O_3$	ESI-	[M-H]-	201	143	45	26	115	45	26
4-Chlorphenoxyacetic acid	$C_8H_7ClO_3$	ESI-	[M-H]-	185	127	24	17	123	24	19
Acetamiprid	$C_{10}H_{11}ClN_4$	ESI +	[M+H]+	223	126	27	20	90	27	35
Amitrole (Aminotriazole)	$C_2H_4N_4$	ESI+	[M+H]+	85	57	15	15	58	15	17
Azimsulfuron	$C_{13}H_{16}N_{10}O_5S$	ESI+	[M+H]+	425	182	52	11	156	52	25
Azocyclotin	$C_{20}H_{35}N_3Sn$	ESI +	[M+NH4]+	455	209	31	29	81	31	35
Bentazone	$C_{10}H_{12}N_2O_3S$	ESI-	[M-H]-	239	132	38	29	196	38	21
Bitertanol	$C_{20}H_{23}N_3O_2$	ESI+	[M+H]+	338	99	31	17	70	31	17
Bromoxynil	$C_7H_3Br_2NO$	ESI-	[M-H]-	274	79	10	11			
Bupirimat	$C_{13}H_{24}N_4O_3S$	ESI +	[M+H]+	317	166	27	23	108	25	25
Buprofenzin	$C_{16}H_{23}N_3OS$	ESI+	[M+H]+	306	201	10	11	106	10	23
Cinidon-ethyl	$C_{19}H_{17}Cl_2NO_4$	ESI+	[M+NH4]+	411	348	10	11	107	10	33
Clethodim	$C_{17}H_{26}ClNO_3S$	ESI+	[M+H]+	360	164	45	17	136	45	33
Clodinafoppropargyl	$C_{17}H_{13}ClFNO_4$	ESI+	[M+H]+	350	266	38	17	91	38	20
Clomazone	$C_{12}H_{14}ClNO_2$	ESI+	[M+H]+	240	125	10	29	89	10	39
Clopyralid	$C_6H_3Cl_2NO_2$	ESI+	[M+H]+	192	146	55	23	110	52	32
Cyazofamid	$C_{13}H_{13}ClN_4O_2S$	ESI+	[M+H]+	325	108	52	13	261	52	9
Cycloxydim	$C_{17}H_{27}NO_3S$	ESI+	[M+H]+	326	280	10	11	180	10	22
Cyhalofop-butyl	$C_{20}H_{20}FNO_4$	ESI+	[M+NH4]+	375	256	38	17	120	38	30
Cyromazine	$C_6H_{10}N_6$	ESI+	[M+H]+	167	85	17	17	125	17	15
Dementon-S-methyl sulfoxid	$C_6H_{15}O_4PS_2$	ESI +	[M+H]+	247	169	33	10	127	18	25
Demeton-S-methyl	$C_6H_{15}O_3PS_2$	ESI +	[M+H]+	231	89	21	5	61	20	25

Demeton-S-methyl sulfon	$C_6H_{15}O_5PS_2$	ESI +	[M+H]+	263	169	55	15	127	45	28
Dichlofenthion	$C_{10}H_{13}Cl_2O_3PS$	ESI+	[M+H]+	315	259	55	17	115	52	45
Dichlorprop (/Dichlorprop-P)	$C_9H_8Cl_2O_3$	ESI-	[M-H]-	233	161	52	17	125	52	26
Diethofencarb	$C_{14}H_{21}NO_4$	ESI +	[M+H]+	268	226	51	15	180	33	17
Dimethomorph	$C_{21}H_{22}ClNO_4$	ESI +	[M+H]+	388	301	45	20	165	23	30
Dinoterb	$C_{10}H_{12}N_2O_5$	ESI-	[M-H]-	239	207	31	23	177	31	25
DNOC	$C_7H_6N_2O_5$	ESI-	[M-H]-	197	137	10	17	109	10	20
Epoxiconazole	$C_{17}H_{13}ClFN_3O$	ESI+	[M+H]+	330	121	45	23	91	45	41
Ethoxyquin	$C_{14}H_{19}NO$	ESI+	[M+H]+	218	148	38	25	174	38	26
Fenamiphos	$C_{13}H_{22}NO_3PS$	ESI+	[M+H]+	304	217	31	23	202	31	33
Fenazaquin	$C_{20}H_{22}N_2O$	ESI+	[M+H]+	307	161	55	17	131	52	14
Fluazifop-p-butyl	$C_{19}H_{20}F_3NO_4$	ESI+	[M+H]+	384	282	38	17	91	38	32
Flumioxazin	$C_{19}H_{15}FN_2O_4$	ESI+	[M+NH4]+	372	355	38	33	299	17	30
Fluoxastrobin	$C_{21}H_{16}ClFN_4O_5$	ESI+	[M+H]+	459	427	45	17	188	45	37
Fluroxypyr	$C_7H_5Cl_2FN_2O_3$	ESI+	[M+H]+	255	181	17	23	209	17	15
Flusilazole	$C_{16}H_{15}F_2N_3Si$	ESI+	[M+H]+	316	165	51	20	247	20	17
Flutolanil	$C_{17}H_{16}F_3NO_2$	ESI +	[M+H]+	324	262	33	35	242	33	25
Hexaconazole	$C_{14}H_{17}Cl_2N_3O$	ESI+	[M+H]+	314	70	24	17	159	24	27
Hexythiazox	$C_{17}H_{21}ClN_2O_2S$	ESI +	[M+H]+	353	228	45	11	168	45	27
Imidacloprid	$C_9H_{10}ClN_5O_2$	ESI +	[M+H]+	256	208	21	15	175	20	20
Iodosulfuron-methyl	$C_{14}H_{13}IN_5NaO_6S$	ESI+	[M+H]+	530	163	21	13	390	21	14
Iprovalicarb	$C_{18}H_{28}N_2O_3$	ESI+	[M+H]+	321	119	45	17	91	45	48
Isoproturon	$C_{12}H_{18}N_2O$	ESI+	[M+H]+	207	72	38	23	165	17	13
Jodfenphos	$C_8H_8Cl_2IO_3PS$	ESI+	[M+H]+	413	287	21	27	143	17	23
Lufenuron	$C_{17}H_8Cl_2F_8N_2O_3$	ESI+	[M+H]+	511	158	33	21	141	33	41
Malaoxon	$C_{10}H_{19}O_7PS$	ESI +	[M+H]+	315	127	48	10	99	33	21
Maleic hydrazide	$C_4H_4N_2O_2$	ESI-	[M-H]-	111	83	55	17	55	23	17
MCPA	$C_9H_9ClO_3$	ESI-	[M-H]-	199	141	55	11	105	55	26
Mecoprop (/Mecoprop-P)	$C_{10}H_{11}ClO_3$	ESI-	[M-H]-	213	141	38	23	105	38	28
Mepanipyrim	$C_{14}H_{13}N_3$	ESI+	[M+H]+	224	106	17	23	77	17	38

Metalaxyl -M	$C_{15}H_{21}NO_4$	ESI+	[M+H]+	280	220	52	11	160	52	22
Methacrifos	$C_7H_{13}O_5PS$	ESI+	[M+NH4]+	258	209	17	11	125	21	25
Methiocarb sulfone	$C_{11}H_{15}NO_4S$	ESI+	[M+NH4]+	275	122	33	25	201	33	10
Methiocarb sulfoxide	$C_{11}H_{15}NO_3S$	ESI+	[M+H]+	242	185	33	10	122	33	30
Metribuzin	$C_8H_{14}N_4S$	ESI+	[M+H]+	215	187	52	23	84	21	20
Metsulfuron-methyl	$C_{14}H_{15}N_5O_6S$	ESI+	[M+H]+	382	167	52	17	135	52	32
Molinate	$C_9H_{17}NOS$	ESI+	[M+H]+	188	126	52	11	83	30	18
Monocrotophos	$C_7H_{14}NO_5P$	ESI +	[M+NH4]+	241	193	21	10	127	10	20
Monolinuron	$C_9H_{11}ClN_2O_2$	ESI+	[M+H]+	215	126	55	17	99	52	30
Nuarimol	$C_{17}H_{12}ClFN_2O$	ESI+	[M+H]+	315	252	55	23	139	52	34
Ofurace	$C_{14}H_{16}ClNO_3$	ESI+	[M+NH4]+	299	254	17	17	160	17	27
Omethoate	$C_5H_{12}NO_4PS$	ESI+	[M+H]+	214	183	10	11	143	10	17
Oxadixyl	$C_{14}H_{18}N_2O_4$	ESI+	[M+H]+	279	219	17	17	132	17	30
Oxycarboxin	$C_{12}H_{13}NO_4S$	ESI+	[M+H]+	268	175	52	17	147	52	22
Pendimethalin	$C_{13}H_{19}N_3O_4$	ESI +	[M+H]+	282	212	33	10	194	33	10
Phosmet	$C_{11}H_{12}NO_4PS_2$	ESI+	[M+NH4]+	335	160	17	17	133	17	45
Picolinafen	$C_{19}H_{12}F_4N_2O_2$	ESI+	[M+H]+	377	256	45	23	238	45	30
Pirimicarb	$C_{11}H_{18}N_4O_2$	ESI+	[M+H]+	239	72	25	16	182	25	14
Propamocarb	$C_9H_{20}N_2O_2$	ESI+	[M+H]+	189	102	24	17	74	24	27
Propargit	$C_{19}H_{26}O_4S$	ESI+	[M+NH4]+	268	231	24	11	175	24	15
Proquinazid	$C_{14}H_{17}IN_2O_2$	ESI +	[M+H]+	373	331	52	11	289	52	25
Prothioconazole	$C_{14}H_{15}Cl_2N_3OS$	ESI+	[M+H]+	344	189	38	17	125	38	36
Pymetrozine	$C_{10}H_{11}N_5O$	ESI +	[M+H]+	218	105	39	25	79	43	40
Pyraclostrobin	$C_{19}H_{18}ClN_3O_4$	ESI+	[M+H]+	388	194	24	11	163	24	25
Pyraflufen-ethyl	$C_{15}H_{13}Cl_2F_3N_2O_4$	ESI+	[M+H]+	413	340	38	11	289	38	27
Pyridaphenthion	$C_{14}H_{17}N_2O_4PS$	ESI +	[M+H]+	341	189	39	30	205	35	18
Pyridate	$C_{19}H_{23}ClN_2O_2S$	ESI+	[M+H]+	379	207	45	17	104	45	30
Pyrimethanil	$C_{12}H_{13}N_3$	ESI+	[M+H]+	200	107	30	25	82	33	27
Pyriproxyfen	$C_{20}H_{19}NO_3$	ESI +	[M+H]+	322	96	55	20	185	27	23
Resmethrin	$C_{22}H_{26}O_3$	ESI +	[M+H]+	339	137	55	15	143	35	23
Rimsulfuron	$C_{14}H_{17}N_5O_7S_2$	ESI +	[M+H]+	432	182	21	15	325	21	13
Spiroxamin	$C_{18}H_{35}NO_2$	ESI +	[M+H]+	298	144	51	20	100	35	30

Tebufenozide	$C_{22}H_{28}N_2O_2$	ESI +	[M+H]+	353	133	24	17	297	24	5
Tebufenpyrad	$C_{18}H_{24}ClN_3O$	ESI+	[M+H]+	334	147	55	23	117	55	30
Tetraconazole	$C_{13}H_{11}Cl_2F_4N_3O$	ESI+	[M+H]+	372	159	45	25	70	30	23
Thifensulfuron-methyl	$C_{12}H_{13}N_5O_6S_2$	ESI-	[M-H]-	386	139	31	25	220	31	5
Thiodicarb	$C_{10}H_{18}N_4O_4S_3$	ESI +	[M+H]+	355	88	27	15	108	27	15
Tri-allate	$C_{10}H_{16}Cl_3NOS$	ESI +	[M+H]+	306	145	24	23	86	24	15
Triasulfuron	$C_{14}H_{16}ClN_5O_5S$	ESI +	[M+H]+	402	167	52	17	141	52	22
Tribenuron-methyl	$C_{15}H_{17}N_5O_6S$	ESI +	[M+H]+	396	155	52	17	181	52	22
Tridemorph	$C_{19}H_{39}NO$	ESI +	[M+H]+	298	130	10	23	98	10	25
Triflumuron	$C_{15}H_{10}ClF_3N_2O_3$	ESI +	[M+H]+	359	156	21	25	139	20	30
Triforine	$C_{10}H_{14}Cl_6N_4O_2$	ESI+	[M+H]+	435	390	17	5	215	17	25
Trinexapac-ethyl	$C_{13}H_{16}O_5$	ESI +	[M+H]+	253	207	52	11	69	52	21

Appendix 2. Repeatability, reproducibility, recovery and limit of detection.

The tables are repeatability, reproducibility and LOD for compounds ionised by ESI- and ESI+, respectively. Values outside the acceptance criteria is marked in italic.

ESI-		**Wheat**			
Concentration, mg/kg		0.02	0.04	0.20	LOD
2-naphtoxy acetic acid	RSD_r, %	27%	19%	2%	
	RSD_R, %	27%	19%	14%	
	Genf.,%	97%	87%	72%	0.016
2,4-D	RSD_r, %			12%	
	RSD_R, %			12%	
	Genf.,%			72%	0.050
4-chlorophenoxyacetic acid	RSD_r, %	20%	14%	6%	
	RSD_R, %	20%	21%	*25%*	
	Genf.,%	111%	105%	70%	0.014
Bentazone	RSD_r, %	21%	15%	3%	
	RSD_R, %	24%	19%	6%	
	Genf.,%	75%	94%	72%	0.011
Bromoxynil	RSD_r, %		17%	*22%*	
	RSD_R, %		18%	*22%*	
	Genf.,%	79%	116%	63%	0.025
Dichlorprop	RSD_r, %	11%	25%	6%	
	RSD_R, %	13%	25%	18%	
	Genf.,%	106%	111%	67%	0.008
Dinoterb	RSD_r, %	19%	11%	7%	
	RSD_R, %	19%	18%	13%	
	Genf.,%	83%	82%	62%	0.009
DNOC	RSD_r, %	14%	17%	8%	
	RSD_R, %	14%	22%	*21%*	
	Genf.,%	80%	81%	*66%*	0.006
MCPA	RSD_r, %	20%	24%	4%	
	RSD_R, %	24%	24%	11%	
	Genf.,%	*148%*	*122%*	79%	0.021
Mecoprop	RSD_r, %		11%	14%	
	RSD_R, %		11%	14%	
	Genf.,%	106%	96%	73%	0.012
Thifensulfuron-methyl	RSD_r, %	17%	26%	10%	
	RSD_R, %	17%	26%	*22%*	
	Genf.,%	*125%*	110%	89%	0.013

Horwitch, %	**29%**	**26%**	**20%**

ESI+		**Wheat**			
Concentration, mg/kg		0.02	0.04	0.20	LOD
Acetamiprid	RSD_r, %			18%	
	RSD_R, %			19%	
	Recov.,%			90%	0.105
Azimsulfuron	RSD_r, %			*21%*	
	RSD_R, %			*21%*	
	Recov.,%			*67%*	0.085
Bitertanol	RSD_r, %			18%	
	RSD_R, %			18%	
	Recov.,%			104%	0.112
Bupirimate	RSD_r, %		26%	10%	
	RSD_R, %		26%	16%	
	Recov.,%		103%	100%	0.032
Buprofenzin	RSD_r, %		21%	14%	
	RSD_R, %		26%	17%	
	Recov.,%		98%	94%	0.030
Clethodim	RSD_r, %			20%	
	RSD_R, %			20%	
	Recov.,%			72%	0.089
Clomazone	RSD_r, %	3%	25%	19%	
	RSD_R, %	25%	25%	19%	
	Recov.,%	102%	98%	101%	0.015
Demeton-S-methyl	RSD_r, %	3%		*35%*	
	RSD_R, %	17%		*35%*	
	Recov.,%	78%	74%	*81%*	0.008
Demeton-S-methyl sulfon	RSD_r, %		11%	17%	
	RSD_R, %		*28%*	17%	
	Recov.,%		91%	98%	0.030
Demeton-S-methyl sulfoxid	RSD_r, %	18%	11%	10%	

	RSD_R, %	28%	24%	19%	
	Recov.,%	107%	*127%*	94%	0.018
Dimethomorph	RSD_r, %	21%	21%	*28%*	
	RSD_R, %	27%	24%	*28%*	
	Recov.,%	95%	107%	92%	0.016
Ethoxyquin	RSD_r, %		17%	19%	
	RSD_R, %		17%	19%	
	Recov.,%		77%	74%	0.016
Fenazaquin	RSD_r, %	21%	22%	9%	
	RSD_R, %	23%	22%	21%	
	Recov.,%	103%	*81%*	*104%*	0.014
Fluoxastrobin	RSD_r, %		17%	12%	
	RSD_R, %		18%	*26%*	
	Recov.,%		94%	90%	0.021
Fluzilafop-p-buthyl	RSD_r, %	23%	13%	13%	
	RSD_R, %	24%	26%	13%	
	Recov.,%	108%	113%	77%	0.015
Iodosulfuron-methyl	RSD_r, %		26%	11%	
	RSD_R, %		26%	11%	
	Recov.,%		*128%*	87%	0.040
Iprovalicarb	RSD_r, %		20%	11%	
	RSD_R, %		23%	11%	
	Recov.,%		66%	84%	0.019
Isoproturon	RSD_r, %		20%	15%	
	RSD_R, %		22%	18%	
	Recov.,%		*95%*	*90%*	0.025
Malaoxon	RSD_r, %	25%	24%	15%	
	RSD_R, %	25%	24%	20%	
	Recov.,%	109%	103%	98%	0.017
Methacrifos	RSD_r, %		26%	5%	
	RSD_R, %		26%	18%	
	Recov.,%		*146%*	107%	0.045
Methalaxyl-M	RSD_r, %	17%	11%	17%	

	RSD_R, %	21%	*15%*	19%	
	Recov.,%	115%	105%	78%	0.015
Methiocarb sulfon	RSD_r, %	18%	26%	*25%*	
	RSD_R, %	24%	26%	*25%*	
	Recov.,%	101%	119%	96%	0.015
Methiocarb sulfoxid	RSD_r, %			6%	
	RSD_R, %			18%	
	Recov.,%			83%	0.091
Metsulfuron-methyl	RSD_r, %	23%	*37%*	13%	
	RSD_R, %	30%	*37%*	19%	
	Recov.,%	88%	*115%*	89%	0.016
Monocrotophos	RSD_r, %		2%	5%	
	RSD_R, %		26%	15%	
	Recov.,%		116%	100%	0.037
Monolinuron	RSD_r, %		20%	10%	
	RSD_R, %		24%	19%	
	Recov.,%		*89%*	*105%*	0.026
Ofurace	RSD_r, %			17%	
	RSD_R, %			19%	
	Recov.,%			89%	0.099
Omethoate	RSD_r, %	18%	4%	16%	
	RSD_R, %	26%	*49%*	16%	
	Recov.,%	100%	90%	101%	0.099
Oxycarboxim	RSD_r, %	24%	20%	16%	
	RSD_R, %	27%	20%	18%	
	Recov.,%	90%	101%	88%	0.015
Pendimethalin	RSD_r, %			19%	
	RSD_R, %			19%	
	Recov.,%			118%	0.135
Pirimicarb	RSD_r, %	18%	12%	7%	
	RSD_R, %	25%	24%	19%	
	Recov.,%	97%	89%	105%	0.013
Propamocarb	RSD_r, %	13%	26%	18%	

	RSD_R, %	17%	26%	*22%*	
	Recov.,%	115%	112%	85%	0.012
Pymetrozin	RSD_r, %	14%	9%	10%	
	RSD_R, %	17%	26%	*22%*	
	Recov.,%	113%	82%	100%	0.011
Pyraclostrobin	RSD_r, %	12%	25%	11%	
	RSD_R, %	23%	25%	20%	
	Recov.,%	88%	93%	86%	0.012
Pyridaben	RSD_r, %			1%	
	RSD_R, %			21%	
	Recov.,%		*83%*	*98%*	0.125
Pyridaphenthion	RSD_r, %	21%	*32%*	6%	
	RSD_R, %	29%	*32%*	16%	
	Recov.,%	80%	83%	74%	0.014
Pyridate	RSD_r, %	26%	26%	6%	
	RSD_R, %	26%	26%	9%	
	Recov.,%	90%	*84%*	*57%*	0.014
Pyrimethanil	RSD_r, %			12%	
	RSD_R, %			18%	
	Recov.,%			103%	0.112
Spiroxamin	RSD_r, %	17%	18%	17%	
	RSD_R, %	30%	18%	20%	
	Recov.,%	85%	90%	78%	0.015
Tebufenpyrad	RSD_r, %		22%	7%	
	RSD_R, %		22%	18%	
	Recov.,%		104%	94%	0.027
$RSD_{Horwitch}$, %		29%	26%	20%	